The existence of time global solutions for tumor invasion models (Nonlinear evolution equations and mathematical modeling)

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The existence of time global solutions for tumor invasion models

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1 Introduction

In this paper, we consider a tumor invasion model with constraint, which is the following systems:

$$
(\mathrm{P}) \begin{cases}
\dfrac{\partial n}{\partial t} = \nabla \cdot \{K_1(\cdot)\nabla n - \lambda n \nabla f\} + \mu n(1-n-f) & \text{in } Q(T) := \Omega \times (0,T), \\
\dfrac{\partial f}{\partial t} = -\delta m f & \text{in } Q(T), \\
\dfrac{\partial m}{\partial t} = K_2(\cdot)\Delta m + C_1 n - C_2 m & \text{in } Q(T), \\
0 \le n + f \le 1, \ m \ge 0, \ f \ge 0, \ n \ge 0 & \text{in } Q(T), \\
n = 0, & \text{in } \Sigma(T) := \Gamma \times (0,T), \\
\dfrac{\partial m}{\partial \mathbf{n}} = 0 & \text{in } \Sigma(T), \\
n(0) = n_0, \ f(0) = f_0, \ m(0) = m_0 & \text{in } \Omega,
\end{cases}
$$

where $0 < T < \infty$; Ω is bounded domain in $\mathbb{R}^N (N = 1,2,3)$ with a smooth boundary $\Gamma = \partial\Omega$; $K_n(\cdot)$ is a non-negative function on $(0,T)$; $\lambda(\cdot)$ is a non-negative function on $Q(T)$; K_m, μ, δ, C_1 and C_2 are positive constants. $\mathbf{n}$ is the outer unit normal vector on Γ; n_0, m_0 and f_0 are initial date. In this model, the unknown functions n, f and m describe the densities of solid tumor cells, the extracellular matrix (denoted by ECM) and the matrix degrading enzymes (denoted by MDE), respectively.

Remark. K_n and K_m are to express that diffusion rate of the tumor cells and MDE, respectively. Originally, they are determined by the state of the protein that exists there.

Therefore, the coefficients must be determined to be dependent on time and space. However, K_n is dependent upon only time.

2 Approach by quasi-variational inequality

First of all, we define the operators which satisfy the following propaties:

1. For each $t \in [0,T]$ and $v \in L^2(Q(T))$, we consider the problem $(\mathrm{P})_m$:

$$(\mathrm{P})_m \begin{cases} \dfrac{\partial \hat{m}}{\partial t} = K_m \Delta \hat{m} + C_1 v - C_2 \hat{m} & \text{in } Q(T), \\ \nabla \hat{m} \cdot \mathbf{n} = 0 \quad \text{on } \Sigma(T), \\ \hat{m}(0) = m_0 \quad \text{in } \Omega. \end{cases}$$

   Then, we denote by $\Lambda_1(t)$ is a solution operator on $L^2(0,T;L^2(\Omega))$ which assigns a unique solution of $(\mathrm{P})_m$ to v, namely, $\hat{m} = \Lambda_1(t)v$.

2. For each $t \in [0,T]$ and $w \in L^2(Q(T))$, we define a function $\Lambda_2(t)w$ by

$$[\Lambda_2(t)w](x,s) := f_0(x) \exp\left(-\delta \int_0^s w(x,\tau)ds\right), \quad \forall (x,s) \in Q(T).$$

   Then, $\Lambda_2(t)$ is a solution operator which assigins a unique solution $\hat{f}$ of the problem $(\mathrm{P})_f$ below to w:

$$(\mathrm{P})_f \begin{cases} \dfrac{\partial \hat{f}}{\partial t} = -\delta \hat{f} w & \text{in } Q(T), \\ \hat{f}(0) = f_0 & \text{in } \Omega. \end{cases}$$

3. For each $t \in [0,T]$ we put $\Lambda(t) := \Lambda_2(t) \circ \Lambda_1(t)$.

Using these operators, we give the diffinition of (P).

Definition 2.1 For each $t \in [0,T]$ a triplet $\{n,f,m\}$ is called a solution of (P) on $[0,t]$ if and only if the following propaties are fulfilled:

(S1) $n \in W^{1,2}(0,t;L^2(\Omega)) \cap L^\infty(0,t;H_0^1(\Omega))$.

(S2) $m = \Lambda_1(t)n, \ f = \Lambda(t)n$.

(S3) $0 \le n \le 1 - f$ a.e. in $Q(T)$,

$$\int_0^t \int_\Omega \left(\frac{\partial n}{\partial s}(s) - \mu n(s)(1 - n(s) - f(s))\right)(n(s) - v(s))dxds$$
$$+ \int_0^t \int_\Omega \left(\lambda(s)\{n(s)\nabla f(s)\} + K_n(s)\nabla n(s)\right) \cdot \nabla(n(s) - v(s))dxds \le 0,$$
$$\text{for } \forall v \in L^2(0,t;H_0^1(\Omega)) \text{ with } 0 \le v \le 1 - f \text{ a.e. in } Q(T).$$

(S4) $n(0) = n_0$ a.e. in Ω.

3 An abstract existence result

In this section, we express about the existence of solution in abstract theory. we use the following notation. Let H be a real Hilbert space equipped with a usual norm $|\cdot|_H$ and an inner product $(\cdot,\cdot)_H$, and X be a real reflexive Banach space, and let X^* be a dual space of X. We assume that X is density and compact imbeded in H.

We consider a nonlinear evolution problem the following formulation

$$\text{(CP)}: \frac{du}{dt}(t) + \partial\varphi^t(u;u(t)) \ni g(t),\ 0<t<T,\ \ u(0)=u_0, \ \text{ in } H,$$

where $\partial\varphi^t(u;\cdot)$ is the subdifferential of covex function $\varphi^t(u;\cdot)$ on H, $u' = \frac{du}{dt}$ and $u_0 : [-\delta_0, 0] \to H$ and $f : (0,T) \to H$ are the initial and forcing functions, respectively. We define the following functional space and its norm; we put

$$\mathcal{V}(-\delta_0,t) := W^{1,2}(-\delta_0,t;H) \cap L^\infty(-\delta_0,t;X),\ 0 \le t \le T.$$
$$|v|_{\mathcal{V}(-\delta_0,t)} := |v|_{L^\infty(-\delta_0,t;X)} + |v'|_{L^2(-\delta_0,t;H)}.$$

This is a sort of functional differential equations generated by subdifferentials of $\varphi^t(v;\cdot)$ with a nonlocal dependence upon v. The objective of this paper is to specify a class of convex functions $\{\varphi^s(v;\cdot)\}_{0\le s\le t}$ as well as its nonlocal dependence upon $v \in \mathcal{V}(-\delta_0,T)$ in order that above Cauchy problrm admits at least one local or global in time solution u.

Definition 3.1(Mosco convergence) Let $\{\varphi_n\}$ be a sequence of proper, lower semicontinuous(l.s.c.), convex functions on X. Then $\{\varphi\}$ converges to a proper, l.s.c., convex function φ on X in the sense of Mosco, if the following two conditons (M1) and (M2) are satisfied:

(M1) Let $\{n_k\}$ be any subsequence of $\{n\}$. If $\{v_k\}$ is a sequence in X and $v \in X$ such that $v_k \to v$ weakly in X as $k \to \infty$, then

$$\liminf_{k\to\infty} \varphi_{n_k}(v_k) \ge \varphi(v).$$

(M2) For each $v \in D(\varphi)$, there is a sequence $\{v_n\}$ in X such that

$$v_n \to v \text{ in } X, \quad \varphi_n(v_n) \to \varphi(v) \text{ as } n \to \infty.$$

For $\forall v \in \mathcal{V}(-\delta_0,t)$ we are given a family $\{\varphi^s(v;\cdot)\}_{0\le s\le t}$ such that

(Φ1) $\varphi^s(v;z)$ is proper, l.s.c., non-negative, convex in $z \in H$; $\varphi^s(v;z)$ is determined by the value of v on $(-\delta_0,s)$, namely $\varphi^s(v_1;z) = \varphi^s(v_2;z)$ wherever $v_1, v_2 \in \mathcal{V}(-\delta_0,t)$, $v_1 = v_2$ on $(-\delta_0,s)$.

(Φ2) $\varphi^s(v;z) \ge C_0|z|_X^p$, $0 \le \forall s \le t$, $\forall v \in \mathcal{V}(-\delta_0,t)$, where $2 \le p < \infty$ and $C_0 > 0$ are constants.

(Φ3) If $0 \le s_n \le t \le T$, $v_n \in \mathcal{V}(-\delta_0,t)$, $s_n \to s$ and $v_n \to v$ weakly in $W^{1,2}(-\delta_0,t;H)$ and weakly$*$ in $L^\infty(-\delta_0,t;X)$, then $\varphi^{s_n}(v_n;\cdot) \to \varphi^s(v;\cdot)$ on H in the sense of Mosco.

Definition 3.2 $u_0 \in C([-\delta_0, 0]; H)$ and $f \in L^2(0,T;H)$. Then we say that u is a solution of the Cauchy problem

$$\text{(CP)} \begin{cases} u'(t) + \partial\varphi^t(u; u(t)) \ni f(t), & 0 < t < T, \text{ in } H, \\ u(t) = u_0(t), & -\delta_0 \le t \le 0, \text{ in } H, \end{cases}$$

if u satisfies that $u \in C([-\delta_0, T]; H)$, $u = u_0$ on $[-\delta_0, 0]$, $u \in W^{1,2}_{loc}((0,T]; H)$, $\varphi^{(\cdot)}(u; u(\cdot)) \in L^1(0,T)$ and $f(t) - u'(t) \in \partial\varphi^t(u; u(t))$ for a.e. $t \in (0,T)$.

Theorem 3.1 Let $0 < T < +\infty$, $0 < \delta_0 < +\infty$, $f \in L^2(0,T;H)$ and $u_0 \in \mathcal{V}(-\delta_0, 0)$ with $\varphi^0(u_0; u_0(0)) < +\infty$. Assume that for all $M > 0$ and $M \le M^* := M^*(f, u_0, \varphi^0(u_0; u_0(0)))$, there are two bounded families $A_M := \{a; v \in \mathcal{V}(-\delta_0, T),\ |v|_{\mathcal{V}(-\delta_0,T)} \le M\}$ of non-negative functions in $L^2(0,T)$ and $B_M := \{b; v \in \mathcal{V}(-\delta_0, T),\ |v|_{\mathcal{V}(-\delta_0,T)} \le M\}$ of non-negative functions in $L^1(0,T)$ such that

(H1) for each $v \in \mathcal{V}(-\delta_0, T)$, $|v|_{\mathcal{V}(-\delta_0,T)} \le M$, $v = u_0$ on $[-\delta_0, 0]$, there exist $a \in A_M$ and $b \in B_M$ with the following property: for each $s, t \in [0,T]$ with $s \le t$ and $z \in D(\varphi^s(v; \cdot))$, there exists $\tilde{z} \in D(\varphi^t(v; \cdot))$ such that

$$\begin{cases} |\tilde{z} - z|_H \le \displaystyle\int_s^t a(\tau)d\tau (1 + \varphi^s(v; z)^{\frac{1}{2}}), \\ \varphi^t(\tilde{z}) - \varphi^s(z) \le \displaystyle\int_s^t b(\tau)d\tau (1 + \varphi^s(v; z)), \end{cases}$$

(H2) for all $\varepsilon > 0$, there exists $\delta_\varepsilon > 0$ such that

$$\int_t^{t+\delta_\varepsilon} (a(s)^2 + b(s))ds < \varepsilon, \ \forall t \in [0, T - \delta_\varepsilon], \ \forall a \in A_M, \ \forall b \in B_M.$$

Then, problem (CP) has at least one solution u on an interval $[0, T']$ with $0 < T' \le T$ such that $u \in \mathcal{V}(-\delta_0, T')$ and $\sup_{0 \le t \le T'} \varphi^t(u; u(t)) < +\infty$.

The detail of of proof is referred to the paper [5].

4 Main result

4.1 Auxiliary equation

In this paper, we give some propositions which is the existence of solutions of auxiliary problem and its estimate. We can directly apply the theory established in [2] to derive Proposition 4.1. So, we omit its proof in this paper.

Proposition 4.1. *(cf. [7]) For each $t \in [0,T]$, $v \in \mathcal{V}(-\delta_0, t)$ and $\hat{n} \in L^\infty(0,T;H_0^1(\Omega))$ the problem*

$$(AP)_{t,v,\hat{n}} \begin{cases} n'(s) + \partial\varphi^s(v; n(s)) \ni G(s, \hat{n}(s), [\Lambda(t)\hat{n}](s)) & \text{in } L^2(\Omega), \quad \text{a.e. } s \in (0,t), \\ n(s) = n_0 \quad \text{in } L^2(\Omega), \quad \forall s \in [-\delta_0, 0]. \end{cases}$$

has a unique solution $n = n_{t,v,\hat{n}} \in W^{1,2}(0,t;L^2(\Omega)) \cap L^\infty(0,t;H_0^1(\Omega))$.

Moreover, there exists a constant $R_1 > 0$, which depends on $\|\kappa_n\|_{C[0,T]}$ and $\|\kappa_n'\|_{L^1(0,T)}$, such that

$$\|n'\|^2_{L^2(Q(T))} + \sup_{0 \le s \le t} \varphi^s(v; n(s)) \le R_1 \left(1 + \|n_0\|^2_{H_0^1(\Omega)} + \|G(\hat{n}, \Lambda(t)\hat{n})\|^2_{L^2(Q(T))}\right),$$

$$\forall t \in [0,T], \quad \forall v \in \mathcal{V}(-\delta_0, t).$$

Lemma 4.1. *There exist a constant $R_2 > 0$ and a non-negative, continuous and strictly increasing function $R_3(\cdot)$ on $[0,T]$ with $R_3(0) = 0$ such that*

$$\|\Lambda(t)\hat{n}\|^2_{L^\infty(0,t;H^3(\Omega))} \le R_2\left(1 + \|f_0\|^2_{H^3(\Omega)}\right)$$

$$+R_3(t)\left(1 + \|m_0\|^2_{H^1(\Omega)} + \|\hat{n}\|^2_{L^\infty(0,T;H_0^1(\Omega))}\right)^2, \quad \forall t \in [0,T].$$

Lemma 4.2. *There exist a constnat $R_4 > 0$ and a continuous, non-negative and strictly increasing function $R_5(\cdot)$ on $[0,T]$ with $R_5(0) = 0$ such that*

$$\|G(\hat{n}, \Lambda(t)\hat{n})\|^2_{L^2(Q(T))} \le R_4\|\mu_n\|^2_{L^2(Q(T))}$$

$$+R_5(t)\left(\|f_0\|^2_{H^3(\Omega)} + 1\right)\left(1 + \|m_0\|^2_{H^2(\Omega)} + \|\hat{n}\|^2_{L^\infty(0,T;H_0^1(\Omega))}\right)^3, \quad \forall t \in [0,T].$$

For each $t \in [0,T]$ and $v \in \mathcal{V}(-\delta_0, t)$, we define the solution operator $S(t,v)$ which assigns a unique solution $S(t,v)\hat{n} := n$ of $(\mathrm{AP})_{t,v,\hat{n}}$ to each $\hat{n} \in L^\infty(-\delta, t; H_0^1)$. We can apply Schauder fixed point theorem, we see that the operator $S(t,v)$ has at least one fixed point. Then, we give the existence theorem as follows:

Proposition 4.2. *There exist a positive constant M_1 and a time $T_0 := T_0(M_1) \in (0,T]$ such that for each $v \in V(-\delta_0, T_0)$ the problem*

$$(AP)_v \begin{cases} n'(t) + \partial\varphi^t(v; n(t)) \ni G(t, n(t), [\Lambda(T_0)n](t)) & \text{in } L^2(\Omega), \quad \text{a.e. } t \in (0,T_0), \\ n(t) = n_0 \quad \text{in } L^2(\Omega), \quad \forall t \in [-\delta_0, 0]. \end{cases}$$

has a unique solution $n_v \in W^{1,2}(0,T_0;L^2(\Omega)) \cap L^\infty(0,T_0;H_0^1(\Omega))$ satisfying

$$\|n_v'\|^2_{L^2(Q_{T_0})} + \sup_{0 \le t \le T_0} \varphi^t(v; n_v(t)) \le M_1. \tag{4.1}$$

Moreover, there exists a positive constant M_2, which is independent of $v \in V(-\delta_0, T_0)$, such that

$$\begin{aligned} &\|[\Lambda_1(T_0)n_v]'\|_{L^2(0,T_0\,;\,H^1(\Omega))} + \|\Lambda_1(T_0)n_v\|_{L^\infty(0,T_0\,;\,H^2(\Omega))} \\ &+\|\Lambda_1(T_0)n_v\|_{L^2(0,T_0\,;\,H^3(\Omega))} + \|\Lambda(T_0)n_v\|_{L^\infty(0,T_0\,;\,H^3(\Omega))} \le M_2. \end{aligned} \tag{4.2}$$

Proof We fix T_0, which is the same number as in Lemma 4.1, and $v \in V(-\delta_0, T_0)$ throughout this argument. Let $\{\hat{n}_k\} \subset \mathcal{W}_{M_1}$ and $\hat{n} \in \mathcal{W}_{M_1}$ so that $\hat{n}_k \longrightarrow \hat{n}$ in $C([0,T];L^2(\Omega))$ as $k \to \infty$. Then, we see that $G(\hat{n}_k, \Lambda(T_0)\hat{n}_k) \longrightarrow G(\hat{n}, \Lambda(T_0)\hat{n})$ weakly in $L^2(Q(T_0))$ as $k \to \infty$. By using the results, we derive $S(T_0,v)\hat{n}_k \longrightarrow S(T_0,v)\hat{n}$ in $C([0,T_0];L^2(\Omega))$, so, $\mathcal{S}(T_0,v)\hat{n}_k \longrightarrow \mathcal{S}(T_0,v)\hat{n}$ in $C([0,T];L^2(\Omega))$ as $k \to \infty$.

By applying Schauder fixed point theorem, we see that $\mathcal{S}(T_0,v)$ has at least one fixed point $\bar{n}$, i.e., $\mathcal{S}(T_0,v)\bar{n} = \bar{n}$, in $\mathcal{W}_{M_1}$. It is clear from the definition of $\mathcal{S}(T_0,v)$ that $\bar{n}$ is a solution of $(\mathrm{AP})_v$ on $[0,T_0]$.

In the rest of this proof, we show the uniqueness of solutions of $(\mathrm{AP})_v$ on $[0,T_0]$. Let n_i $(i=1,2)$ be solutions of $(\mathrm{AP})_v$ on $[0,T_0]$. For simplicity, we put $\theta_i := \Lambda(T_0)n_i$ and $\zeta_i := \Lambda_1(T_0)n_i$.

First of all, we note that ζ_i $(i=1,2)$ satisfies the following system:

$$(\zeta_1-\zeta_2)' - \kappa_m\Delta(\zeta_1-\zeta_2) + C_3(\zeta_1-\zeta_2) = C_2(n_1-n_2) \quad \text{a.e. in } Q(T_0), \tag{4.3}$$

$$\nabla(\zeta_1-\zeta_2)\cdot\nabla\boldsymbol{n} = 0 \quad \text{a.e. on } \Sigma_{T_0}, \tag{4.4}$$

$$(\zeta_1-\zeta_2)(0) = 0 \quad \text{a.e. in } \Omega. \tag{4.5}$$

We multiply (4.3) by $\zeta_1-\zeta_2$ and ∇(4.3) by $\nabla(\zeta_1-\zeta_2)$. By integrating these resultants over $Q(T_0)$, it is easily seen that there exists a constant $K_{22} > 0$ such that

$$\begin{aligned} &\sup_{0\le s\le t}\|\zeta_1(s)-\zeta_2(s)\|^2_{H^1(\Omega)} + \int_0^t \|\zeta_1(s)-\zeta_2(s)\|^2_{H^2(\Omega)}ds \\ &\le K_1\int_0^t \|n_1(s)-n_2(s)\|^2_{H^1_0(\Omega)}ds, \quad \forall t \in [0,T_0]. \end{aligned} \tag{4.6}$$

In order to show the uniqueness of solutions of $(\mathrm{AP})_v$ on $[0,T_0]$, we have to estimate the term $(G(n_1,\theta_1)-G(n_2,\theta_2), n_1-n_2)_{L^2(\Omega)}$ by the following ways.

(1) It is easily seen from (4.2) that for any $\varepsilon_1 > 0$ there exists a constant $K_2(\varepsilon) > 0$ such that the following inequality holds for a.e. $t \in (0,T_0)$:

$$\begin{aligned} &\int_\Omega |\nabla n_1(x,t) - \nabla n_2(x,t)||\nabla\theta_1(x,t)||n_1(x,t)-n_2(x,t)|dx \\ &\le \varepsilon_1\|n_1(t)-n_2(t)\|^2_{H^1_0(\Omega)} + K_2(\varepsilon_1)\|n_1(t)-n_2(t)\|^2_{L^2(\Omega)}. \end{aligned}$$

(2) By using (4.1), (4.2) and (4.6), we see that for any $\varepsilon_2 > 0$ there exists a constant

$K_3(\varepsilon_2) > 0$ such that the following inequality holds for a.e. $t \in (0, T_0)$:

$$\begin{aligned}
&\int_\Omega |\nabla n_2(x,t)||\nabla\theta_1(x,t) - \nabla\theta_2(x,t)||n_1(x,t) - n_2(x,t)|dx \\
\leq\ & C_1 \int_\Omega |\nabla n_2(x,t)||\nabla f_0(x)||n_1(x,t) - n_2(x,t)| \left(\int_0^t |\zeta_1(x,s) - \zeta_2(x,s)|ds\right) dx \\
&+C_1^2 \int_\Omega |\nabla n_2(x,t)||n_1(x,t) - n_2(x,t)| \\
&\qquad\times \left(\int_0^t |\zeta_1(x,s) - \zeta_2(x,s)|ds\right)\left(\int_0^t |\nabla\zeta_1(x,s)|ds\right) dx \\
&+C_1 \int_\Omega |\nabla n_2(x,t)||n_1(x,t) - n_2(x,t)| \left(\int_0^t |\nabla\zeta_1(x,s) - \nabla\zeta_2(x,s)|ds\right) dx
\end{aligned}$$

$$\begin{aligned}
\leq\ & C_1\|\nabla f_0\|_{C(\overline{\Omega})}\|n_2(t)\|_{H_0^1(\Omega)}\|n_1(t) - n_2(t)\|_{L^4(\Omega)} \int_0^t \|\zeta_1(t) - \zeta_2(t)\|_{L^4(\Omega)}ds \\
&+C_1^2\|n_2(t)\|_{H_0^1(\Omega)} \int_0^t \|\nabla\zeta_1(s)\|_{C(\overline{\Omega})}ds \\
&\qquad\times\|n_1(t) - n_2(t)\|_{L^4(\Omega)} \int_0^t \|\zeta_1(t) - \zeta_2(t)\|_{L^4(\Omega)}ds \\
&+C_1\sqrt{T_0}\|n_2(t)\|_{H_0^1(\Omega)}\|n_1(t) - n_2(t)\|_{L^4(\Omega)} \left(\int_0^t \|\nabla\zeta_1(s) - \nabla\zeta_2(s)\|_{L^4(\Omega)}^2ds\right)^{\frac{1}{2}} \\
\leq\ & \varepsilon_2\|n_1(t) - n_2(t)\|_{H_0^1(\Omega)}^2 + K_3(\varepsilon_2)\int_0^t \|n_1(s) - n_2(s)\|_{H_0^1(\Omega)}^2ds.
\end{aligned}$$

(3) It is easily seen that for any $\varepsilon_3 > 0$ there exists a constant $K_4(\varepsilon_3) > 0$ such that the following inequality holds for a.e. $t \in (0, T_0)$:

$$\begin{aligned}
&\int_\Omega |\Delta\theta_1(x,t)||n_1(x,t) - n_2(x,t)|^2dx \\
\leq\ & \|\Delta\theta_1(t)\|_{L^4(\Omega)}\|n_1(t) - n_2(t)\|_{L^4(\Omega)}\|n_1(t) - n_2(t)\|_{L^2(\Omega)} \\
\leq\ & \varepsilon_3\|n_1(t) - n_2(t)\|_{H_0^1(\Omega)}^2 + K_4(\varepsilon_3)\|n_1(t) - n_2(t)\|_{L^2(\Omega)}^2.
\end{aligned}$$

(4) It is easily seen that for any $\varepsilon_4 > 0$ there exists a constant $K_5(\varepsilon_4) > 0$ such that the

following inequality holds for a.e. $t \in (0, T_0)$:

$$
\begin{aligned}
&\int_\Omega |n_2(x,t)||\Delta\theta_1(x,t) - \Delta\theta_2(x,t)||n_1(x,t) - n_2(x,t)|dx \\
\le\ & C_1 \int_\Omega |\Delta f_0(x)||n_1(x,t) - n_2(x,t)| \left(\int_0^t |\zeta_1(x,s) - \zeta_2(x,t)|ds \right) dx \\
&+2C_1^2 \int_\Omega |\nabla f_0(x)||n_1(x,t) - n_2(x,t)| \left(\int_0^t |\nabla\zeta_1(x,s)|ds \right) \\
&\qquad \times \left(\int_0^t |\zeta_1(x,s) - \zeta_2(x,s)|ds \right) dx \\
&+2C_1 \int_\Omega |\nabla f_0(x)||n_1(x,t) - n_2(x,t)| \left(\int_0^t |\nabla\zeta_1(x,s) - \nabla\zeta_2(x,s)|ds \right) dx \\
&+C_1^3 \int_\Omega |n_1(x,t) - n_2(x,t)| \left(\int_0^t |\nabla\zeta_1(x,s)|ds \right)^2 \left(\int_0^t |\zeta_1(x,s) - \zeta_2(x,s)|ds \right) dx \\
&+C_1^2 \int_\Omega |n_1(x,t) - n_2(x,t)| \left(\int_0^t |\nabla\zeta_1(x,s)|ds + \int_0^t |\nabla\zeta_2(x,s)|ds \right) \\
&\qquad \times \left(\int_0^t |\nabla\zeta_1(x,s) - \nabla\zeta_2(x,s)|ds \right) dx \\
&+C_1^2 \int_\Omega |n_1(x,t) - n_2(x,t)| \left(\int_0^t |\Delta\zeta_1(x,s)|ds \right) \left(\int_0^t |\zeta_1(x,s) - \zeta_2(x,s)|ds \right) dx \\
&+C_1 \int_\Omega |n_1(x,t) - n_2(x,t)| \left(\int_0^t |\Delta\zeta_1(x,s) - \Delta\zeta_2(x,s)|ds \right) dx \\
\le\ & C_1 \|\Delta f_0\|_{L^4(\Omega)} \|n_1(t) - n_2(t)\|_{L^4(\Omega)} \int_0^t \|\zeta_1(s) - \zeta_2(s)\|_{L^2(\Omega)} ds \\
&+2C_1^2 \|\nabla f_0\|_{C(\overline{\Omega})} \int_0^t \|\zeta_1(s)\|_{H^1(\Omega)} ds \\
&\qquad \times \|n_1(t) - n_2(t)\|_{L^2(\Omega)} \int_0^t \|\zeta_1(s) - \zeta_2(s)\|_{H^2(\Omega)} ds \\
&+2C_1 \|\nabla f_0\|_{C(\overline{\Omega})} \|n_1(t) - n_2(t)\|_{L^2(\Omega)} \int_0^t \|\zeta_1(s) - \zeta_2(s)\|_{H^1(\Omega)} ds \\
&+C_1^3 \left(\int_0^t \|\nabla\zeta_1(s)\|_{C(\overline{\Omega})} ds \right) \|n_1(t) - n_2(t)\|_{L^2(\Omega)} \int_0^t \|\zeta_1(s) - \zeta_2(s)\|_{L^2(\Omega)} ds \\
&+C_1^2 \left(\int_0^t \|\nabla\zeta_1(s)\|_{C(\overline{\Omega})} ds + \int_0^t \|\nabla\zeta_2(s)\|_{C(\overline{\Omega})} ds \right) \\
&\qquad \times \|n_1(t) - n_2(t)\|_{L^2(\Omega)} \int_0^t \|\zeta_1(s) - \zeta_2(s)\|_{H^1(\Omega)} ds
\end{aligned}
$$

$$+C_1^2\left(\int_0^t \|\zeta_1(s)\|_{H^2(\Omega)}ds\right)\|n_1(t)-n_2(t)\|_{L^2(\Omega)}\int_0^t \|\zeta_1(s)-\zeta_2(s)\|_{C(\overline{\Omega})}ds$$

$$+C_1\|n_1(t)-n_2(t)\|_{L^2(\Omega)}\int_0^t \|\zeta_1(s)-\zeta_2(s)\|_{H^2(\Omega)}ds$$

$$\leq \varepsilon_4\|n_1(t)-n_2(t)\|^2_{H_0^1(\Omega)}+K_5(\varepsilon_4)\int_0^t \|n_1(s)-n_2(s)\|^2_{H_0^1(\Omega)}ds.$$

(5) It is easily seen that there exists a constant $K_6>0$ such that the following inequality holds for a.e. $t\in(0,T)$:

$$\int_\Omega \mu_n(x,t)\left[n_1(x,t)\{1-n_1(x,t)-\theta_1(x,t)\}-n_2(x,t)\{1-n_2(x,t)-\theta_2(x,t)\}\right]$$

$$\times\{n_1(x,t)-n_2(x,t)\}dx$$

$$\leq \|\mu_n(t)\|_{L^\infty(\Omega)}\left(4\|n_1(t)-n_2(t)\|^2_{L^2(\Omega)}+\int_\Omega|\theta_1(t)-\theta_2(t)||n_1(t)-n_2(t)|dx\right)$$

$$\leq K_6\|\mu_n(t)\|_{L^\infty(\Omega)}\left(\|n_1(t)-n_2(t)\|^2_{L^2(\Omega)}+\int_0^t \|\zeta_1(s)-\zeta_2(s)\|^2_{L^2(\Omega)}ds\right).$$

We see from (1)–(5) that there exist constants $K_i>0$ ($i=7,\ 8$) such that

$$\frac{d}{dt}\Psi(t)\leq K_7\left(1+\|\mu_n(t)\|_{L^\infty(\Omega)}\right)\Psi(t),\quad \text{a.e. } t\in(0,T_0), \tag{4.7}$$

where

$$\Psi(t):=\|n_1(t)-n_2(t)\|^2_{L^2(\Omega)}+K_8\int_0^t \|n_1(s)-n_2(s)\|^2_{H_0^1(\Omega)}ds.$$

By applying Gronwall lemma, we derive $n_1(t)=n_2(t)$ in $L^2(\Omega)$ for all $t\in[0,T_0]$, i.e., the uniqueness of solution of $(\mathrm{AP})_v$ on $[0,T_0]$. ∎

4.2 Local existence of solutions

In this section, we state our main theorem of the present paper, which gives the existence of time-local solutions of (P), and show its proof.

Theorem 4.1. *(P) has at least one solution $[n,f,m]$ on $[0,T_0]$, where T_0 is the same time as in Proposition 4.2.*

Throughout this section, let M_1 and T_0 be the same constants as in Proposition 4.1. In order to show Theorem 4.1, we define a non-empty, closed and convex subset $\mathcal{W}_{M_1}(T_0)$ of $C([0,T_0];L^2(\Omega))$, and an operator $\mathcal{L}$ from $\mathcal{W}_{M_1}(T_0)$ into itself by

$$\mathcal{W}_{M_1}(T_0):=\left\{v\in\mathcal{V}_{T_0}^+\ \middle|\ \|v'\|_{L^2(Q(T_0))}+\sup_{0\leq t\leq T_0}\varphi_0(v(t))\leq M_1\right\}$$

and

$$\mathcal{L}v:=n_v,\quad \forall v\in\mathcal{W}_{M_1}(T_0),$$

respectively. Actually, it is easily seen from Proposition 4.1 that the operator $\mathcal{L}$ is well-defined on $\mathcal{W}_{M_1}(T_0)$.

Now, we give the proof of Theorem 4.1 below.

Proof of Theorem 4.1. Let $\{v_k\} \subset \mathcal{W}_{M_1}(T_0)$ and $v \in \mathcal{W}_{M_1}(T_0)$ so that

$$v_k \longrightarrow v \quad \begin{cases} \text{in } C([0,T_0];L^2(\Omega)), \\ \text{weakly in } W^{1,2}(0,T_0;L^2(\Omega)), \\ *\text{-weakly in } L^\infty(0,T_0;H_0^1(\Omega)) \cap L^\infty(Q(T_0)). \end{cases}$$

For simplicity, for each $k \in \mathbf{N}$ we put $\bar{n}_k := \mathcal{L}v_k$, $m_k := \Lambda_1(T_0)\bar{n}_k$ and $f_k := \Lambda(T_0)\bar{n}_k$. Then, it is easily seen from the definition of $\mathcal{W}_{M_1}(T_0)$ that there exist a subsequence of $\{k\}$, which is denoted by the same notation $\{k\}$, and $\bar{n} \in \mathcal{W}_{M_1}(T_0)$ such that the following convergences hold:

$$\bar{n}_k \longrightarrow \bar{n} \quad \begin{cases} \text{in } C([0,T_0];L^2(\Omega)), \\ \text{weakly in } W^{1,2}(0,T_0;L^2(\Omega)), \\ *\text{-weakly in } L^\infty(0,T_0;H_0^1(\Omega)) \cap L^\infty(Q(T_0)). \end{cases} \tag{4.8}$$

By using the continuity property of $\Lambda_1(T_0)$, we see that the following convergences hold:

$$m_k \longrightarrow \Lambda_1(T_0)\bar{n} \quad \begin{cases} \text{in } C([0,T_0];H^1(\Omega)) \cap L^2(0,T_0;H^2(\Omega)), \\ \text{weakly in } W^{1,2}(0,T_0;H^1(\Omega)) \cap L^2(0,T_0;H^3(\Omega)), \\ *\text{-weakly in } L^\infty(0,T_0;H^2(\Omega)). \end{cases} \tag{4.9}$$

By repeating the similar argument, we see that the following convergence holds:

$$G(\bar{n}_k, f_k) \longrightarrow G(\bar{n}, \Lambda(T_0)\bar{n}) \quad \text{weakly in } L^2(Q(T_0)). \tag{4.10}$$

In the rest of this proof, we show that n is a solution of $(\mathrm{AP})_v$ on $[0,T_0]$.

For this, we let z any function in $L^2(0,T_0;H_0^1(\Omega))$ satisfying $0 \le z \le 1 - \Lambda(T_0)v$ a.e. in $Q(T_0)$ and put $z_k := \min\{z, 1-\Lambda(T_0)v_k\}$. Since z_k satisfies $0 \le z_k \le 1 - \Lambda(T_0)v_k$ a.e. in $Q(T_0)$, it is easily seen that the following inequality holds:

$$\begin{aligned} &\int_0^{T_0} (\bar{n}_k'(t), \bar{n}_k(t) - z_k(t))dt + \int_0^{T_0}\int_\Omega \kappa_n(t)\nabla\bar{n}_k(x,t)\cdot\nabla(\bar{n}_k(x,t) - z_k(x,t))dxdt \\ &\qquad \le \int_0^{T_0} (G(\bar{n}_k(t), f_k(t)), \bar{n}_k(t) - z_k(t))dt. \end{aligned} \tag{4.11}$$

By taking $\lim_{k\to\infty}$ in (4.11) and using (4.8)–(4.10) with $z_k \longrightarrow z$ in $L^2(0,T_0;H_0^1(\Omega))$, we see that the following inequaity holds:

$$\begin{aligned} &\int_0^{T_0} (\bar{n}'(t), \bar{n}(t) - z(t))dt + \int_0^{T_0}\int_\Omega \kappa_n(t)\nabla\bar{n}(x,t)\cdot\nabla(\bar{n}(x,t) - z(x,t))dxdt \\ &\qquad \le \int_0^{T_0} (G(\bar{n}(t), [\Lambda(T_0)\bar{n}](t)), \bar{n}(t) - z(t))dt, \end{aligned} \tag{4.12}$$

which implies that $\bar{n}$ is a solution of $(\mathrm{AP})_v$ on $[0, T_0]$, i.e., $\bar{n} = \mathcal{L}v$. Hence, we see that the operator $\mathcal{L} : \mathcal{W}_{M_1}(T_0) \longrightarrow \mathcal{W}_{M_1}(T_0)$ is continuous with respect to the strong topology of $C([0, T_0]; L^2(\Omega))$.

By applying Schauder fixed point theorem, we see that $\mathcal{L}$ has at least one fixed point, namely, there exists $n \in \mathcal{W}_{M_1}(T_0)$ such that $\mathcal{L}n = n$. It is clear from the definition of $\Lambda(T_0)$ and $\Lambda_1(T_0)$ that a triplet $[n, \Lambda(T_0)n, \Lambda_1(T_0)n]$ is a solution of (P) on $[0, T_0]$. ■

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